Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (currently amended) A fibronectin type III (Fn3) polypeptide monobody comprising:

at least two Fn3 β-strand domain sequences with a loop region sequence linked between adjacent β-strand domain sequences; and

optionally, an N-terminal tail of at least about 2 amino acids, a C-terminal tail of at least about 2 amino acids, or both;

wherein at least one loop region sequence, the N-terminal tail, or the C-terminal tail comprises an amino acid sequence which varies by deletion, insertion, or replacement of at least two amino acids from a corresponding loop region, N-terminal tail, or C-terminal tail in a tenth Fn3 domain of fibronectin having the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:3, and

wherein the polypeptide monobody exhibits nuclear receptor binding activity.

2. (original) The polypeptide monobody according to claim 1, wherein the nuclear receptor is selected from the group consisting of steroid receptors, thyroid receptors, retinoid receptors, vitamin D receptors, and orphan nuclear receptors.

3. (original) The polypeptide monobody according to claim 2, wherein the nuclear receptor is a steroid receptor.

4. (previously presented) The polypeptide monobody according to claim 3, wherein the steroid receptor is an estrogen receptor, an androgen receptor, a progestin receptor, a glucocorticoid receptor, or a mineralocorticoid receptor.

5. (original) The polypeptide monobody according to claim 4, wherein the steroid receptor is an estrogen receptor.

6. (original) The polypeptide monobody according to claim 5, wherein the polypeptide monobody exhibits estrogen receptor binding activity in the presence of an estrogen receptor agonist or an estrogen receptor antagonist.

7. (original) The polypeptide monobody according to claim 6, wherein the estrogen receptor agonist is estradiol, estriol, diethylstilbestrol, or genistein.

8. (original) The polypeptide monobody according to claim 6, wherein the estrogen receptor antagonist is hydroxy tamoxifen, ICI182780, or raloxifene.

9. (previously presented) The polypeptide monobody according to claim 1, wherein said at least two Fn3 β-strand domain sequences comprises β-strand domain sequences A through G of a tenth Fn3 domain of human fibronectin or derivatives thereof, wherein the loop region sequences comprise an AB loop, a BC loop, a CD loop, a DE loop, an EF loop, and an FG loop.

10. (previously presented) The polypeptide monobody according to claim 9, wherein the at least one loop region sequence is selected from the group consisting of the AB loop region sequence, the BC loop region sequence, the DE loop region sequence, the FG loop region sequence, and combinations thereof.

11. (original) The polypeptide monobody according to claim 9, wherein the at least one loop region sequence is a combination of the BC loop region sequence and the FG loop region sequence.

12. (cancelled)

13. (original) A fusion protein comprising:

a first portion comprising a polypeptide monobody according to claim 1 and

a second portion fused to the first portion.

14. (original) The fusion protein according to claim 13, wherein the second portion comprises a label.

15. (original) The fusion protein according to claim 14, wherein the label is an alkaline phosphatase tag or a $His_{(6)}$ tag.

16. (original) The fusion protein according to claim 13, wherein the second portion comprises a transcriptional activation domain.

17–144. (cancelled)

145. (withdrawn) A method of validating nuclear receptor protein activity comprising:

exposing a nuclear receptor protein to a polypeptide monobody according to claim 1 which binds to the nuclear receptor protein and

determining whether binding of the nuclear receptor protein by the polypeptide monobody modifies nuclear receptor protein activity.

146. (withdrawn) The method according to claim 145, wherein said exposing is carried out *in vivo*.

147. (withdrawn) The method according to claim 146, wherein said exposing is carried out in a yeast cell, bacterial cell, or mammalian cell.

148. (withdrawn) The method according to claim 145, wherein said determining comprises:

detecting mRNA or protein expression levels prior to said exposing and after said exposing and

comparing the detected mRNA or protein expression levels to identify proteins that are downstream of the pathway of the nuclear receptor protein, wherein modified expression levels indicated modified nuclear receptor protein activity.

149. (withdrawn) The method according to claim 145, wherein the nuclear receptor protein is required for cell growth or survival, said determining comprising:

measuring cell growth or survival after said exposing, wherein reduced cell growth or survival indicates inhibition of nuclear receptor protein activity.

150. (withdrawn) The method according to claim 145, wherein the nuclear receptor protein is a pathogen protein involved in host-pathogen interaction, said exposing comprising:

exposing a host cell comprising the polypeptide monobody to the pathogen.

151. (withdrawn) The method according to claim 150, wherein said determining comprises:

determining the extent of pathogen-induced disease progression in the host cell.

152. (withdrawn) The method according to claim 150, wherein the pathogen is a bacteria.

153. (withdrawn) A method of measuring polypeptide monobody binding affinity for a nuclear receptor protein, said method comprising:

exposing a nuclear receptor protein to (i) an interaction partner that binds the nuclear receptor protein, and (ii) a polypeptide monobody according to claim 1 that binds the nuclear receptor protein; and

measuring the degree to which the polypeptide monobody competes with the interaction partner.

154. (withdrawn) The method according to claim 153, wherein said exposing is carried out *in vitro*.

155. (withdrawn) The method according to claim 154, wherein the nuclear receptor protein is bound to a substrate.

156. (withdrawn) The method according to claim 154, wherein the polypeptide monobody comprises a label.

157. (withdrawn) The method according to claim 156, wherein the label is an alkaline phosphatase tag or a $His_{(6)}$ tag.

158. (withdrawn) The method according to claim 153, wherein said exposing is carried out *in vivo*.

159. (withdrawn) A method of modulating nuclear receptor protein activity comprising:

exposing a nuclear receptor protein to a polypeptide monobody according to claim 1 that binds the nuclear receptor protein under conditions effective to modify nuclear receptor protein activity.

160. (withdrawn) The method according to claim 159, wherein said exposing is carried out *in vivo*.

161. (withdrawn) The method according to claim 160, wherein said exposing is carried out in a yeast cell, bacterial cell, or mammalian cell.

162. (withdrawn) The method according to claim 159, wherein the nuclear receptor is selected from the group consisting of steroid receptors, thyroid receptors, retinoid receptors, vitamin D receptors, and orphan nuclear receptors.

163. (withdrawn) The method according to claim 162, wherein the nuclear receptor is a steroid receptor.

164. (withdrawn) The method according to claim 163, wherein the steroid receptor is an estrogen receptor, an androgen receptor, a progestin receptor, a glucocorticoid receptor, or a mineralocorticoid receptor.

165. (withdrawn) The method according to claim 164, wherein the steroid receptor is an estrogen receptor.

166. (withdrawn) A method of detecting conformation of a nuclear receptor protein, said method comprising:

exposing a nuclear receptor protein to a polypeptide monobody according to claim 1 that interacts with the nuclear receptor protein when the nuclear receptor protein is in a specific conformation, under conditions effective for the polypeptide monobody to interact with the nuclear receptor protein, and

determining whether the polypeptide monobody interacts with the nuclear receptor protein, wherein interaction between the polypeptide monobody and the nuclear receptor protein indicates that the nuclear receptor protein is in the specific conformation.

167. (withdrawn) The method according to claim 166, wherein said exposing is carried out *in vitro*.

168. (withdrawn) The method according to claim 167, wherein the nuclear receptor protein is bound to a substrate.

169. (withdrawn) The method according to claim 167, wherein the polypeptide monobody comprises a label.

170. (withdrawn) The method according to claim 169, wherein the label is an alkaline phosphatase tag or a $His_{(6)}$ tag.

171. (withdrawn) The method according to claim 166, wherein said exposing is carried out *in vivo*.

172. (withdrawn) The method according to claim 171, wherein said exposing is carried out in a yeast cell, bacterial cell, or mammalian cell.

173. (withdrawn) The method according to claim 166, wherein the nuclear receptor is selected from the group consisting of steroid receptors, thyroid receptors, retinoid receptors, vitamin D receptors, and orphan nuclear receptors.

174. (withdrawn) The method according to claim 173, wherein the nuclear receptor is a steroid receptor.

175. (withdrawn) The method according to claim 174, wherein the steroid receptor is an estrogen receptor, an androgen receptor, a progestin receptor, a glucocorticoid receptor, or a mineralocorticoid receptor.

176. (withdrawn) The method according to claim 175, wherein the steroid receptor is an estrogen receptor.

177. (withdrawn) A method of detecting a change in conformation of a nuclear receptor protein, said method comprising:

(i) detecting conformation of a nuclear receptor protein according to the method of claim 166; and

(ii) repeating said detecting after a time delay to determine whether the nuclear receptor protein binds to a different polypeptide monobody or to the same polypeptide monobody but with a different degree of interaction;

wherein binding to a different polypeptide monobody or a change in degree of interaction with the same polypeptide monobody indicates change in conformation of the nuclear receptor protein.

178. (withdrawn) The method according to claim 177, further comprising exposing the nuclear receptor protein to a ligand prior to step (ii).

179. (withdrawn) The method according to claim 178, wherein said exposing is carried out *in vitro*.

180. (withdrawn) The polypeptide monobody according to claim 1, wherein the FG loop region sequence comprises the amino acid sequence selected from the group of SEQ ID NO: 20 and SEQ ID NO: 32.

181. (withdrawn) The polypeptide monobody according to claim 1, wherein the BC loop region sequence comprises the amino acid sequence selected from the group of SEQ ID NO: 22, SEQ ID NO: 23, and SEQ ID NO: 24.

182. (withdrawn) The polypeptide monobody according to claim 1, wherein the FG loop region sequence comprises the amino acid sequence selected from the group of SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 72, and SEQ ID NO: 73.

183. (withdrawn) The polypeptide monobody according to claim 1, wherein the AB loop region sequence comprises the amino acid sequence selected from the group of SEQ ID NO: 34 and SEQ ID NO: 35.

184. (cancelled)

185. (new) A fibronectin type III (Fn3) polypeptide monobody comprising β-strand domain sequences A through G of a tenth Fn3 domain of fibronectin, and loop region sequences AB, BC, CD, DE, EF, and FG, wherein at least one loop region sequence selected from the group of AB, BC, FG, and combinations thereof, varies by deletion, insertion, or replacement of at least two amino acids from a corresponding loop region in the tenth Fn3 domain of fibronectin, and wherein the polypeptide monobody exhibits nuclear receptor binding activity.